Hormone therapy revisited

The last shots in the hormone replacement therapy (HRT) battle have not been fired, but the big guns of large randomised clinical trials (RCTs) are rapidly neutralising myths that have persisted for decades. Two articles in this journal keep up the pressure in favour of evidence-based medicine. Rosenberg and Hoffman (p. 26) may appear to take a more abolitionist stance, but they argue mainly against the use of HRT for disease prevention. Davey (p. 23) argues more pragmatically on the basis of the importance of symptom control.

Findings from several large RCTs provide important major conclusions, including:

- Postmenopausal HRT should not be used to reduce the risk for coronary heart disease events for women with coronary heart disease.
- Evidence strongly supports that initiating HRT in women with previous venous thromboembolism probably increases the risk of recurrent venous thomboembolism.
- Oestradiol does not reduce the mortality or the recurrence of stroke in postmenopausal women with cerebrovascular disease and should not be used for its prevention.
- Breast cancer was significantly increased by HRT, and it was more advanced in such cases.
- The incidence of colorectal cancer decreases with HRT.
- Hip fractures were reduced by HRT.
- The incidence of dementia was increased in HRT users relative to placebo (thus going against suggestions that quality of life and brain function are improved by the use of HRT).

Davey notes that the relief of menopausal symptoms is the prime overwhelming need for many, if not most, postmenopausal women. The relief of postmenopausal symptoms was not included in the Women's Health Initiative trial. Relief of symptoms must be given due weight in any assessment of the benefits and risks of HRT. He concludes that the balance of benefits and risks in individual women varies greatly. HRT must be individual, and each woman has to come to a personal decision with the help and advice of her clinician.

Chloroquine blindness

With the increase in the incidence of malaria in our region the use of antimalarials has been increasing. Many clinicians will be surprised to hear that many patients in South Africa develop profound visual loss every year as a result of chloroquine toxicity. Kelvin Rivett addresses this important matter (p. 41) and proposes a solution to the problem.

Chloroquine is used as prophylaxis against malaria and is also prescribed for the treatment of amoebiasis, rheumatoid arthritis, etc. It is excreted from the body very slowly and becomes concentrated in the melanin-containing cells of the retinal pigment epithelium and choroid. Most cases of toxicity occur when a higher than recommended dose is used. Retinal toxicity and degeneration occur and are a severe sight-threatening complication of chloroquine use. The chloroquine daily dose is thought to be more important than the cumulative dose and should be tailored according to gender and height.

Chloroquine-related blindness has been almost completely eradicated in countries where hydroxychloroquine is freely available. Rivett strongly advocates such a switch in South Africa.

Haemophilus influenzae vaccines

We are reminded that *Haemophilus influenzae* type b (HiB) remains the principal cause of invasive bacterial diseases in under-5-year-olds in developing countries. Vaccines have proved to be effective in reducing transmission rates and protecting the children at risk from invasive HiB disease, in the developing countries in which the HiB vaccines are now used.

Matjila and colleagues (p. 43) compared the safety and immunogenicity of two vaccines, VaxemHib and HibTITER. They followed the World Health Organisation's accelerated schedule which allows 4-week intervals between the doses. They concluded that both vaccines showed comparable safety and immunogenicity when administered to South African babies at 6, 10 and 14 weeks of age.

Resistance to malaria

Severe malaria in the Comoros Union and in Madagascar is invariably caused by *Plasmodium falciparum*, as it is in the rest of sub-Saharan Africa. Barnes and Folb, in an editorial, address the complexities of measuring the resistance to malaria (p. 46) in response to an article from Madagascar (p. 47). The latter submit, on the basis of their findings, that current policy for the treatment of severe malaria with a 7-day course of quinine, and prophylaxis with either mefloquine or cycloguanil-based regimens, are justified by their *in vitro* laboratory findings.

As malaria morbidity and mortality are rising, principally as the result of increasing antimalarial resistance, Barnes and Folb evaluate the interesting and important conclusions. They address the use of the drugs and the various factors that encourage the spread of resistance, including the proportion of transmissible malaria infections exposed to sub-therapeutic concentrations of drug, the drug concentration profile, the pattern of drug use, and the level of immunity in the community. Resistance frequently develops first to the antimalarials most widely used in the treatment of uncomplicated malaria.

In vitro testing does not allow for drug behaviour in the body — the absorption, metabolism, distribution and elimination characteristics that significantly affect the antimalarial action of drugs. Nor can it take into account the complex immune response that takes place in conjunction with the drug action.

Laboratory methods would have to be standardised, and more general agreement is needed on how *in vitro* laboratory findings might be used in deciding on policy change and in comparing the situation between countries and regions.

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